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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/890,567	04/02/2002	Frank Larsen	p0282776	4584

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EXAMINER	
MYERS, CARLA J	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 09/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/890,567	LARSEN ET AL.	
	Examiner	Art Unit	
	Carla Myers	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34-65* is/are pending in the application.

4a) Of the above claim(s) *51-60* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34-50 and 61-65* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/2/01*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group 1 in the reply filed on August 18, 2004 is acknowledged. The traversal is on the ground(s) that the special technical feature linking the claims is not only the solid phase that binds telomerase but also a telomerase specific oligonucleotide primer. It is stated that the Hardingham reference does not teach using the solid phase to bind telomerase, nor does the reference teach a telomerase specific primer. This is not found persuasive because the technical feature linking the claimed inventions is not in fact a solid phase that binds telomerase and a telomerase specific primer. Claim 1 of Group 1 does not require the use of a telomerase specific primer. Further, independent claim 51 of Group 2 does not specifically require a telomerase specific primer. Thereby the combination of reagents of a solid phase that binds telomerase and a telomerase specific primer does not link the inventions of Groups 1 and 2. If one did consider that a combination of reagents linked the inventions of Group 1 and 2, then that combination of reagents would be a solid phase that binds telomerase and any reagent that could be used to assay for telomerase activity. Hardingham does teach reagents that have the property of being useful for the detection of telomerase activity. Specifically, Hardingham teaches methods which require the use of the PCR reagents, including DNA polymerase and dNTPs. DNA polymerase and dNTPs have the property of being useful for assaying for telomerase activity. Secondly, there is no requirement for Hardingham to teach that the solid support may be used to bind telomerase. Hardingham teaches a solid support which

has each of the same broadly recited structural and functional properties of the solid phase required by the present claims. Thereby, the reagent of a solid support that binds telomerase or the combination of reagents of a solid support that binds telomerase and dNTPs does not constitute a special technical feature because these reagents are taught by the prior art of Hardingham.

The requirement is still deemed proper and is therefore made FINAL.

Specification

2. The specification is objected to because the assigned SEQ ID NOs have not been used to identify each sequence listed, as required under 37 CFR §1.821(d). See for example, pages 2, 38 and 39 of the specification.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 34-65 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 34-40 and 42-50 are indefinite over the recitation of "assaying the test sample" because it is not clear as to what constitutes the test sample. The claims include a step of separating the solid phase from the treated sample to form a test sample. However, it is unclear as to whether the test sample consists of the solid phase having telomerase bound thereto or consists of the sample eluted from the solid phase or consists of the material in the test sample that did not bind to the solid support.

Claims 34-40 are indefinite over the recitation in (c) of "the sample" because it is not clear as to whether this refers to the "sample from a human or animal subject," "the treated sample," or the "test sample." Similarly, claim 35 is indefinite over the recitation of "wherein **the sample** comprises..."

Claims 34-50 are indefinite because there is not a nexus between the preamble of the claims and the process steps set forth in the claims. The claims are drawn to methods for cancer diagnosis or prognosis. However, the claims recite the final step of assaying for telomerase activity "wherein detection of telomerase activity in the sample is indicative of cancer in the subject." Since prognosis refers to the likely outcome or course of a disease, detecting cancer in a subject is not equivalent to "cancer prognosis." The claims do not clarify how the step of detecting telomerase activity also results in determining the prognosis of a patient. Accordingly, it is not clear as to whether the claims are intended to be limited to methods for detecting cancer in a subject or to methods for cancer diagnosis and prognosis.

Claim 44 is indefinite over the recitation of "wherein the detection of telomerase activity in the sample is further indicative of micrometastasis" because there is not a nexus between the preamble of the claim and the method steps recited in the claim. Claim 44 recites a method for cancer diagnosis or prognosis. It is not clear as to whether detection of micrometastasis is considered to be a means for accomplishing the prognosis of a patient or is distinct from determining a patient's prognosis. The claims do not clarify the relationship between the diagnosis and prognosis of cancer and the determination of micrometastasis. Thereby, it is unclear as to whether the method is

intended to be one which diagnosis or prognosis cancer or one which detects cancer and micrometastasis. Further, it is not clear as to whether "the sample" refers to the "sample from a human or animal subject," "the treated sample," or the "test sample."

Claims 61-65 are indefinite and vague over the recitation of "using the solid phase to bind telomerase." The recitation of "using" renders the claims indefinite because it is not clear as to how the solid phase is to be used to bind telomerase. It is unclear as to whether the claims are intended to include an actual step of binding telomerase to a solid phase or if the "using" step allows for the non-specific binding and removal of telomerase from a reaction mixture. It is also unclear as to what is intended to be the relationship between the step of using the solid support to bind telomerase and the step of assaying for telomerase activity.

Claim 65 is indefinite over the recitation of "the particulate material" because this phrase lacks proper antecedent basis. It appears that the claim should refer back to claim 62, rather than claim 61.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claim 61 is rejected under 35 U.S.C. 102(e) as being anticipated by Morin (U.S. Patent No. 6,767,719).

Morin teaches that telomerase activity is associated with the occurrence of cancer that the presence of telomerase activity can be used as a means for diagnosing cancer (see, for example, columns 3, 13 and 50). Morin (columns 44-48 and 50-51) also teaches several methods for detecting telomerase activity. In particular, Morin (column 45) teaches a method for "Detecting Telomerase Activity Using Immobilized Enzyme." In this method, "telomerase activity is monitored in a solid-phase system using the so-called catalyzed reporter deposition (CARD) system. Telomerase enzyme or mTERT is immobilized onto a solid phase using the antibodies of the invention or chemical linkers, and the like. To assay full [sic] or a "partial" mTERT or telomerase enzyme activity, a telomerase enzymatic reaction is carried out in a buffered aqueous solution compatible with the assayed telomerase activity. The appropriate reagents are added to detect the activity, for example, to allow the telomerase to catalyze multiple copies multiple copies of detectable, reaction product." Accordingly, Morin teaches a method comprising providing a solid support for binding telomerase and reagents for assaying for telomerase activity, using the solid support to bind telomerase, and assaying for telomerase activity.

With respect to the recitation in the claims of "providing a kit," the method of Morin is considered to be one in which a kit is provided since the method of Morin requires providing the reagents of a solid phase and components to detect telomerase activity and these reagents are provided in containers that allow for their use in the

laboratory. It is noted that in the absence of any recitation in the claims or any direction in the specification to the contrary, the recitation of kit reads on component parts capable of being assembled or a plurality of elements grouped together as a kit. Accordingly, the word "kit" does not impart any additional special structural or functional features which distinguishes the claimed method over that of Morin.

5. Claim 61-65 are rejected under 35 U.S.C. 102(e) as being anticipated by Weinrich (W) 98/45450).

Weinrich teaches methods for purifying telomerase using a solid support and methods for detecting telomerase activity. It is stated that "In methods of purifying telomerase it is often useful to determine the presence or amount of telomerase in a preparation" (page 13). Weinrich (pages 22-23) teaches that telomerase may be immobilized onto a solid support by contacting a sample containing telomerase with a solid phase having an affinity reagent attached thereto. The affinity reagent may be an antibody or a RNA or DNA sequence that binds to telomerase. Following binding of telomerase to the affinity agent, unbound molecules are separated or removed from the mixture and then telomerase is released from the affinity agent/support (see page 23). Weinrich (page 32-33) also states that "Antibodies that specifically recognize telomerase or a telomerase associated protein are also useful for detecting the presence of these proteins in a sample, such as a cell or tissue. Because telomerase is present in most cancers, the identification of telomerase aids in the diagnosis of cancer or pre-cancerous states. Detecting the presence of telomerase with antibodies is inexpensive and offers speed and ease." Weinrich (page 55-56) exemplifies methods of

immobilizing and purifying telomerase using MPG® Streptavidin beads, which are known to be 5 micrometer magnetic beads. Once the telomerase is released from the support, the released material is assayed for telomerase activity. Accordingly, Weinrich teaches a method comprising the steps of providing a solid support for binding telomerase and reagents for assaying for telomerase activity, using the solid support to bind telomerase, and assaying for telomerase activity.

With respect to the recitation in the claims of "providing a kit," the method of Weinrich is considered to be one in which a kit is provided since the method of Weinrich requires providing the reagents of a solid phase and components to detect telomerase activity and these reagents are provided in containers that allow for their use in the laboratory. It is noted that in the absence of any recitation in the claims or any direction in the specification to the contrary, the recitation of kit reads on component parts capable of being assembled or a plurality of elements grouped together as a kit. Accordingly, the word "kit" does not impart any additional special structural or functional features which distinguishes the claimed method over that of Morin.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 34, 35, 40, 41 and 61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morin.

Morin teaches that telomerase activity is associated with the occurrence of cancer that the presence of telomerase activity can be used as a means for diagnosing cancer (see, for example, columns 3, 13 and 50). Morin (columns 44-48 and 50-51) also teaches several methods for detecting telomerase activity. In particular, Morin (column 45) teaches a method for "Detecting Telomerase Activity Using Immobilized Enzyme." In this method, "telomerase activity is monitored in a solid-phase system using the so-called catalyzed reporter deposition (CARD) system. Telomerase enzyme or mTERT is immobilized onto a solid phase using the antibodies of the invention or chemical linkers, and the like. To assay full [sic] or a "partial" mTERT or telomerase enzyme activity, a telomerase enzymatic reaction is carried out in a buffered aqueous solution compatible with the assayed telomerase activity. The appropriate reagents are added to detect the activity, for example, to allow the telomerase to catalyze multiple

copies multiple copies of detectable, reaction product." Accordingly, Morin teaches a method comprising providing a solid support for binding telomerase and reagents for assaying for telomerase activity, using the solid support to bind telomerase, and assaying for telomerase activity. With respect to the recitation in the claims of "providing a kit," the method of Morin is considered to be one in which a kit is provided since the method of Morin requires providing the reagents of a solid phase and components to detect telomerase activity and these reagents are provided in containers that allow for their use in the laboratory. It is noted that in the absence of any recitation in the claims or any direction in the specification to the contrary, the recitation of kit reads on component parts capable of being assembled or a plurality of elements grouped together as a kit. Accordingly, the word "kit" does not impart any additional special structural or functional features which distinguishes the claimed method over that of Morin.

With respect to claim 61, if the term "kit" is intended to impart a specific structural limitation, it is noted that Morin also teaches packaging the reagents required to detect telomerase and telomerase activity into a kit (see, for example, column 6). Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have practiced the method of Morin using a specifically designed kit containing a solid support for binding telomerase and reagents for detecting telomerase activity for the benefits of the convenience and cost-effectiveness offered by kits.

With respect to claims 34, 35, 39 and 41, Morin does not exemplify as a single embodiment a method in which cancer is diagnosed by first binding telomerase to a solid phase and detecting telomerase activity as indicative of the occurrence of cancer.

However, Morin does teach methods for diagnosing cancer by detecting telomerase activity and teaches that telomerase activity may be assayed using the catalyzed reporter deposition (CARD) system and immobilized telomerase. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have used the catalyzed reporter deposition system of Morin in a method for detecting telomerase activity in a patient's test sample in order to have provided an effective means for detecting telomerase activity in patient's samples which would have allowed for the rapid and effective diagnosis of cancer. In view of the teachings of Morin of how to perform CARD and how to perform telomerase activity assays, such a method would have necessarily included the steps of lysing a cell to release telomerase, binding telomerase to a solid support, removing unbound reagents, and assaying for the presence of telomerase activity as indicative of cancer in the subject.

Additionally, Morin (column 35) teaches alternative methods for detecting telomerase activity. Morin states that telomerase may be detected or quantified by functional activity assays, by immunological assays and by nucleic acid based techniques. For example, at columns 35-37, Morin teaches that the anti-telomerase antibodies immobilized onto a solid support may be used to bind to and detect the presence of telomerase in a sample. The reference teaches that such immunological binding assays will include wash steps after each combination of reagents is added

(column 38). It is noted that the present claims are considered to include methods of detecting telomerase protein as a means of "assaying the test sample for telomerase activity" since the presence of telomerase is correlated with telomerase activity Further, it is noted that the present specification at pages 37- 38 indicates that telomerase RNA may be detected as indicative of telomerase activity. Thereby, the claims are considered to include methods which indirectly assay for enzyme activity by detecting the presence of telomerase. Accordingly, it have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Morin so as to have diagnosed cancer by performing an assay in which a sample of cells were lysed to release telomerase, telomerase was immobilized onto a solid phase having a telomerase affinity reagent bound thereto, and the presence of telomerase bound to the solid phase was detected as indicative of the presence of telomerase activity in the sample and the presence of cancer. One would have been motivated to have generated such a method in order to have provided a rapid and effective means for diagnosing cancer.

With respect to claim 40, Morin (column 46) also teaches that telomerase activity can be detected using the well known TRAP assay. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have further modified the method of Morin so as to have performed the CARD method wherein telomerase activity was determined using the TRAP assay because this would have provided an effective means for determining the presence or quantity of telomerase activity in the test sample as indicative of cancer.

7. Claims 36-39 and 62-65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morin in view of Weinrich (WO 98/45450).

The teachings of Morin are presented above. Morin does not specify the type of solid support used to immobilize telomerase.

However, Weinrich teaches methods for detecting telomerase activity and methods for purifying telomerase. Weinrich (pages 22-23) teaches that telomerase may be immobilized onto a solid support by contacting a sample containing telomerase with a solid phase having an affinity reagent attached thereto. The affinity reagent may be an antibody or a RNA or DNA sequence that binds to telomerase. Following binding of telomerase to the affinity agent, unbound molecules are separated or removed from the mixture and then telomerase is released from the affinity agent/support (see page 23). Weinrich (page 32-33) also states that "Antibodies that specifically recognize telomerase or a telomerase associated protein are also useful for detecting the presence of these proteins in a sample, such as a cell or tissue. Because telomerase is present in most cancers, the identification of telomerase aids in the diagnosis of cancer or pre-cancerous states. Detecting the presence of telomerase with antibodies is inexpensive and offers speed and ease." Weinrich (page 55-56) exemplifies methods of immobilizing and purifying telomerase using MPG® Streptavidin beads, which are known to be 5 micrometer magnetic beads.

In view of the teachings of Weinrich, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Morin so as to have immobilized the telomerase onto MPG® Streptavidin beads

coated with telomerase RNA or anti-telomerase antibody in order to have provided an effective and convenient means for immobilizing and separating telomerase from other cellular components by magnetic separation.

8. Claims 42-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morin in view of Dahm (U.S. Patent 6,582,904).

The teachings of Morin are presented above. Morin does not teach performing a step of sorting a mixture of cells using a solid phase having bound thereto an affinity reagent for target cells.

Dahm teaches methods for diagnosing and prognosing cancer by detecting the presence of telomerase activity. The reference (columns 6-7) teaches: "To prevent or reduce false-positive results or so-called background noise which is caused by telomerase activities which are possibly present in nontumor cells, it is advantageous to purify the body fluid which has been taken before the novel investigation. The intention is, in particular, to deplete stem cells and/or activated immune cells, or concentrate tumor cells, in the sample to be investigated." Dahm (column 7) teaches that tumor cells can be concentrated or stem cells and activated immune cells removed using magnetic beads having attached thereto antibodies against specific surface markers present on these cells. The reference also teaches that the sample to be analyzed may be any body fluid, including urine, stool or blood (column 2).

In view of the teachings of Dahm, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Morin so as to have concentrated the tumor cells from a body sample or to have removed

stem cells or activated immune cells from the body sample prior to lysing the target cells and assaying for telomerase activity in order to have prevented or reduced false-positive results thereby providing a more accurate and sensitive method for diagnosing cancer. Additionally, it would have been obvious to have used an affinity reagent specific for epithelial cells in circumstances in which the type of cell to be assayed for telomerase was limited to epithelial cells, e.g. breast cancer epithelial cells, in order to have provided an effective means for enriching targeted epithelial cells and thereby improving the accuracy of the cancer detection method.

8. Claims 34-41 and 61-65 are rejected under 35 U.S.C. 103(a) as being unpatentable Weinrich.

This rejection is applied to claims 61-65 based on the interpretation that the term "kit" is intended to impart a specific structural limitation.

Weinrich teaches methods for purifying telomerase using a solid support and methods for detecting telomerase activity. The reference (page 2) states that "Assays for telomerase are useful in characterizing cancer cells or pre-cancer cells, because most cancer cells express telomerase." Weinrich teaches the advantages of obtaining purified telomerase, including the fact that purified telomerase is more useful than crude extracts for studying the enzymes activity and mechanisms. It is stated that "In methods of purifying telomerase it is often useful to determine the presence or amount of telomerase in a preparation" (page 13). Weinrich (pages 22-23) teaches that telomerase may be immobilized onto a solid support by contacting a sample containing telomerase with a solid phase having an affinity reagent attached thereto. The affinity reagent may

be an antibody or a RNA or DNA sequence that binds to telomerase. Following binding of telomerase to the affinity agent, unbound molecules are separated or removed from the mixture and then telomerase is released from the affinity agent/support (see page 23). Weinrich (page 32-33) also states that "Antibodies that specifically recognize telomerase or a telomerase associated protein are also useful for detecting the presence of these proteins in a sample, such as a cell or tissue. Because telomerase is present in most cancers, the identification of telomerase aids in the diagnosis of cancer or pre-cancerous states. Detecting the presence of telomerase with antibodies is inexpensive and offers speed and ease." Weinrich (page 55-56) exemplifies methods of immobilizing and purifying telomerase using MPG® Streptavidin beads, which are known to be 5 micrometer magnetic beads. Once the telomerase is released from the support, the released material is assayed for telomerase activity. Accordingly, Weinrich teaches a method comprising the steps of providing a solid support for binding telomerase and reagents for assaying for telomerase activity, using the solid support to bind telomerase, and assaying for telomerase activity. Weinrich does not teach performing the detection method using a specific compartmentalized kit containing a solid support that binds telomerase and reagents for assaying for telomerase. However, reagent kits for performing detection methods were conventional in the diagnostic arts at the time the invention was made. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have practiced the method of Weinrich using a specifically designed kit containing a solid support for binding

telomerase and reagents for detecting telomerase activity for the benefits of the convenience and cost-effectiveness offered by kits.

With respect to claims 34-41, Weinrich does not exemplify as a single embodiment a method in which cancer is diagnosed by first binding telomerase to a solid phase, removing unbound material and detecting telomerase activity as indicative of the occurrence of cancer. However, Weinrich does disclose methods for diagnosing cancer wherein the methods comprise detecting telomerase activity as indicative of the occurrence of cancer. Further, Weinrich teaches that antibodies bound to a solid support can be used to isolate telomerase and that this provides a means for detecting the presence of telomerase and telomerase activity. The reference also teaches that once telomerase has been purified from a cell source, telomerase activity can be detected using the TRAP assay (page 12).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have generated a method for detecting telomerase activity in a patient's sample wherein the method comprised lysing a cell sample from a patient, isolating telomerase protein using a solid support having an anti-telomerase antibody or telomerase specific nucleic acid bound thereto, removing unbound cellular materials, and then assaying for the presence of telomerase activity by directly detecting telomerase. One would have been motivated to have done so in order to have accomplished the benefits set forth by Weinrich of providing an effective, inexpensive and rapid means for detecting telomerase activity as indicative of the presence of cancer. It is noted that the present claims are considered to include methods of

detecting telomerase protein as a means of "assaying the test sample for telomerase activity" since the presence of telomerase is correlated with telomerase activity. Further, it is noted that the present specification at pages 37- 38 indicates that telomerase RNA may be detected as indicative of telomerase activity. Thereby, the claims are considered to include methods which indirectly assay for enzyme activity by detecting the presence of telomerase.

Further, it was well known in the art at the time the invention was made that reagents present in cellular extracts could potentially interfere with the enzymatic activity of telomerase. Therefore, the ordinary artisan would have recognized that providing a pure sample of telomerase protein would have improved the accuracy of the method for detecting the enzymatic activity of telomerase since such cellular components would be absent from the reaction mixture. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have generated a method for detecting telomerase activity in a test sample wherein the method comprised lysing a cell sample from a subject, isolating telomerase protein using a solid support having an anti-telomerase antibody or telomerase specific nucleic acid bound thereto, removing unbound cellular material, and then assaying for the presence of telomerase activity by performing an enzyme assay such as the TRAP assay. One would have been motivated to have generated this method in order to have provided a more accurate means for directly assaying the enzyme activity of telomerase in order to effectively diagnose or prognose cancer.

9. Claims 42-50 are rejected under 35 U.S.C. 103(a) as being unpatentable Weinrich in view of Dahm.

The teachings of Weinrich are presented above. Weinrich does not teach performing a step of sorting a mixture of cells using a solid phase with an affinity reagent for target cells.

Dahm teaches methods for diagnosing and prognosing cancer by detecting the presence of telomerase activity. The reference (columns 6-7) teaches: "To prevent or reduce false-positive results or so-called background noise which is caused by telomerase activities which are possibly present in nontumor cells, it is advantageous to purify the body fluid which has been taken before the novel investigation. The intention is, in particular, to deplete stem cells and/or activated immune cells, or concentrate tumor cells, in the sample to be investigated." Dahm (column 7) teaches that tumor cells can be concentrated or stem cells and activated immune cells removed using magnetic beads having attached thereto antibodies against specific surface markers present on these cells. The reference also teaches that the sample to be analyzed may be any body fluid, including urine, stool or blood (column 2).

In view of the teachings of Dahm, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Weinrich so as to have concentrated the tumor cells from a body sample or to have removed stem cells or activated immune cells from the body sample prior to lysing the target cells and assaying for telomerase activity in order to have prevented or reduced false-positive results thereby providing a more accurate and sensitive method for

diagnosing cancer. Additionally, it would have been obvious to have used an affinity reagent specific for epithelial cells in circumstances in which the type of cell to be assayed for telomerase was limited to epithelial cells, e.g. breast cancer epithelial cells, in order to have provided an effective means for enriching targeted epithelial cells and thereby improving the accuracy of the cancer detection method.

10. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

The CPG Inc. Online catalog (1997) teaches that MPG® Streptavidin comprises an aqueous suspension of 5 micrometer superparamagnetic particles covalently coupled to streptavidin.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is (571) 272-0747. The examiner can normally be reached on Monday-Thursday from 6:30 AM-5:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (571)-272-0782.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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Carla Myers
September 8, 2004

CARLA J. MYERS
PRIMARY EXAMINER